

We claim:

1. A method of diagnosing myelinopathy in an individual comprising the steps of:

obtaining a sample containing nucleic acid from said individual;  
assaying said sample for an alteration in a periaxin polynucleotide, wherein said alteration is associated with said myelinopathy.

2. The method of claim 1, wherein said periaxin polynucleotide is SEQ ID NO:1.

3. The method of claim 1, wherein said periaxin polynucleotide is SEQ ID NO:1, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, or SEQ ID NO:77.

4. The method of claim 1, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy syndrome (RLS).

5. The method of claim 1, wherein said assaying step further comprises a polymerase chain reaction.

6. The method of claim 5, wherein primers for said polymerase chain reaction are selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID

NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, and SEQ ID NO:26.

7. The method of claim 1, wherein said alteration is 3775G>A, 1216G>A, 4075-4077d, 1483G>C, 3394A>G, 3248C>G, 2763A>G, 2645C>T, 306C>T, 1491C>G, 2655T>C, 2145T>A, or 247ΔC.

8. A method of diagnosing myelinopathy in an individual comprising the steps of:

obtaining a sample containing protein from said individual;

assaying said sample for an alteration in a periaxin polypeptide, wherein said alteration is associated with said myelinopathy.

9. The method of claim 8, wherein said periaxin polypeptide is SEQ ID NO:2.

10. The method of claim 8, wherein said periaxin polypeptide is SEQ ID NO:2, SEQ ID NO:88, or SEQ ID NO:89.

11. The method of claim 8, wherein said periaxin polypeptide is SEQ ID NO:2, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, or SEQ ID NO:93.

12. The method of claim 8, wherein said alteration is E1259K, A406T, E1359delΔ, E495Q, R1132G, P1083R, I921M, A882V, T102T, P497P, P885P, R953X, R368X, S929fsX957, R196X, V763fsX774, C715X, or R82fsX96.

13. The method of claim 8, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy Syndrome (RLS).

14. As a composition of matter, a defect of a periaxin polynucleotide that is 3775G>A, 1216G>A, 4075-4077d, 1483G>C, 3394A>G, 3248C>G, 2763A>G, 2645C>T, 306C>T, 1491C>G, 2655T>C, 2145T>A, or 247ΔC.

15. As a composition of matter, a defect of a periaxin polypeptide that is E1259K, A406T, E1359Δ, E495Q, R1132G, P1083R, I921M, A882V, T102T, P497P, P885P, C715X, or R82fsX96.

16. As a composition of matter, a defect of periaxin polypeptide that is E1259K, A406T, E1359delΔ, E495Q, R1132G, P1083R, I921M, A882V, T102T, P497P, P885P, R953X, R368X, S929fsX957, R196X, V763fsX774, C715X, or R82fsX96.

17. A method of identifying a compound for the treatment of myelinopathy comprising the steps of:

exposing said compound to a knockout animal, wherein said animal comprises at least one defective allele of a periaxin polynucleotide and wherein said animal has at least one symptom associated with said myelinopathy; and assaying for an improvement in said at least one symptom of said myelinopathy after exposure to said compound.

18. The method of claim 17, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy Syndrome (RLS).

19. A method of screening for a compound for the treatment of myelinopathy comprising the steps of:

providing a cell lacking a functional periaxin amino acid sequence; contacting said cell with said compound; and determining the effect of said compound on said cell, wherein said effect on said cell is indicative of said treatment of said myelinopathy.

20. The method of claim 19, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy Syndrome (RLS).

21. A method of identifying an upregulator of periaxin nucleic acid sequence expression comprising the steps of:

administering a test compound to a transgenic animal, wherein the genome of said transgenic animal comprises a reporter nucleic acid sequence, wherein said sequence is under the control of an operably linked periaxin promoter active in eukaryotic cells;

measuring the level of said periaxin expression; and

comparing the level of said periaxin expression in said animal with normal periaxin expression, wherein an increase in said level following administration of said test compound indicates said test compound is an upregulator.

22. A method of identifying a drug having activity in the treatment of myelinopathy, comprising the steps of:

obtaining a compound suspected of having extracellular signaling activity; and determining whether said compound has said extracellular signaling activity.

23. The method of claim 22, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy Syndrome (RLS).

24. A method of treating myelinopathy in an organism, comprising the step of administering to said organism a therapeutically effective amount of a periaxin nucleic acid sequence, wherein said nucleic acid sequence is administered by a vector.

25. The method of claim 24, wherein said vector is selected from the group consisting of a plasmid, a viral vector, a lipid, a liposome, a polypeptide, or a combination thereof.

26. The method of claim 24, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to

pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy Syndrome (RLS).

27. A method of treating myelinopathy in an organism comprising the step of administering to said organism a therapeutically effective amount of a periaxin amino acid sequence, wherein said amino acid sequence is administered with a physiologically acceptable carrier.

28. The method of claim 27, wherein said myelinopathy is Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), or Roussy-Levy Syndrome (RLS).

29. A method of treating an animal for a myelinopathy comprising the steps of:  
identifying a compound which interacts with a periaxin periaxin; and  
administering to said animal a therapeutically effective amount of said compound.

30. The method of claim 29, wherein said myelinopathy is Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), or Roussy-Levy Syndrome (RLS).

31. A method of treating a patient for a myelinopathy comprising the steps of:  
preparing a compound obtained by the method of claim 17, 19, 21, or 22; and  
administering said compound with a physiologically acceptable carrier to said patient.

32. A kit for diagnosing a myelinopathy in an animal comprising at least two primers, wherein one primer is specific to a sense periaxin nucleic acid sequence and another primer is specific to an antisense periaxin nucleic acid sequence.

33. The kit of claim 32, wherein said primers are SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID

NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26.

34. As a composition of matter, a nucleic acid sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26.

35. A method of detecting the presence or absence of a mutation associated with a myelinopathy, the method comprising:

- a) isolating a test nucleic acid from a subject, said test nucleic acid comprising a periaxin polynucleotide;
- b) comparing the test nucleic acid to a reference wild-type periaxin polynucleotide; and
- c) determining the differences between the test nucleic acid and the reference wild-type periaxin polynucleotide, wherein the differences are mutations in the periaxin polynucleotide of the subject, and wherein the presence of a mutation in the periaxin polynucleotide of the subject is indicative of the presence of the myelinopathy in the subject.

36. The method of claim 35, wherein said mutation is 3775G>A, 1216G>A, 4075-4077d, 1483G>C, 3394A>G, 3248C>G, 2763A>G, 2645C>T, 306C>T, 1491C>G, 2655T>C, 2145T>A, or 247ΔC.

37. The method of claim 35, wherein said mutation encodes a defect of a periaxin polypeptide, wherein the defect is E1259K, A406T, E1359delΔ, E495Q, R1132G, P1083R, I921M, A882V, T102T, P497P, P885P, R953X, R368X, S929fsX957, R196X, V763fsX774, C715X, or R82fsX96.

38. The method of claim 35, wherein said periaxin polynucleotide is SEQ ID NO:1, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ

ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, or SEQ ID NO:77.

39. The method of claim 35, wherein said comparing step is by DHPLC, sequencing, hybridization, or a combination thereof.

40. The method of claim 35, wherein the myelinopathy is Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), or Roussy-Levy Syndrome (RLS).